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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/824,187	04/13/2004	Michael Samoszuk	034827-0203	7086

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EXAMINER	
FREDMAN, JEFFREY NORMAN	
ART UNIT	**PAPER NUMBER**
1637	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/13/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/824,187	SAMOSZUK ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 January 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-8* is/are pending in the application.

4a) Of the above claim(s) *8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Newly submitted claim 8 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Claim 8 is drawn to a method of using claim 3. Inventions of claim 8 and the product of claims 3-7 are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case, the product can be used in multiple different methods, including DGGE, nucleic acid purification, or nucleic acid hybridization, so method and product are distinct. Further, a search of both groups, the method and product group, would be burdensome because the search would involve different search terms, different concepts and would utilize different databases and different analyses.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 8 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Interpretation

2. The newly added limitation "wherein said DNA molecule has a predetermined melting profile" has no structural impact on the product claim. This is solely a recitation of purpose, without structure. Every nucleic acid inherently has some melting profile, so

the only issue is whether a method step of determining has occurred. This has no structural effect on the product. As the Federal Circuit noted in Abbott Laboratories v. Baxter Pharmaceutical Products Inc., 80 USPQ2d 1860, 1863 (Fed. Cir. 2006), "Our cases have consistently held that a reference may anticipate even when the relevant properties of the thing disclosed were not appreciated at the time."

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 3-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Tok et al (J. American Academy of Dermatology (March 1998) 38(3):453-460).

Tok teaches a composition comprising:

a) a substantially pure DNA molecule comprising a TCR gene sequence (see page 455, subheading "PCR", where the TCR gamma gene is amplified by PCR primers to result in a pure sequence)

b) a buffer suitable for loading on a TTGE gel (see page 455, column 2, where the PCR product is concentrated to 10 ul and mixed with loading dye, specifically 0.4% bromophenol blue, 0.4% xylene cyanol and 25% Ficoll).

With regard to claim 4, Tok teaches a GC- clamp (see page 455, column 2, where Tok teaches a GC-clamp attached to the primers).

With regard to claim 5, Tok teaches tha tthe TCR gene sequence may be derived from a rearranged TCRgamma gene (see page 455, column 1, "PCR for the TCR gamma, gene rearrangement was performed by modifying a previously published protocol by means of these primers").

With regard to claim 6, Tok teaches a TCR primer amplified using a primer complementary to the V region of the TCR gene (see page 455, column 1) and a primer complementary to the J region of the TCR gene (see page 455, column 2).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Tok et al (J. American Academy of Dermatology (March 1998) 38(3):453-460) in view of Littman et al (Nature (1987) 326:85-88) and further in view of Buck et al (Biotechniques (1999) 27(3):528-536).

Tok teaches a composition comprising:

a) a substantially pure DNA molecule comprising a TCR gene sequence (see page 455, subheading "PCR", where the TCR gamma gene is amplified by PCR primers to result in a pure sequence)

b) a buffer suitable for loading on a TTGE gel (see page 455, column 2, where the PCR product is concentrated to 10 ul and mixed with loading dye, specifically 0.4% bromophenol blue, 0.4% xylene cyanol and 25% Ficoll).

With regard to claim 4, Tok teaches a GC- clamp (see page 455, column 2, where Tok teaches a GC-clamp attached to the primers).

With regard to claim 5, Tok teaches tha tthe TCR gene sequence may be derived from a rearranged TCRgamma gene (see page 455, column 1, "PCR for the TCR gamma, gene rearrangement was performed by modifying a previously published protocol by means of these primers").

With regard to claim 6, Tok teaches a TCR primer amplified using a primer complementary to the V region of the TCR gene (see page 455, column 1) and a primer complementary to the J region of the TCR gene (see page 455, column 2).

Littman teaches a composition comprising:

a) a substantially pure DNA molecule comprising a TCR gene sequence as shown below

```
   1 gaatcaggaa gaccagctcc tcctactgtc ttctgtgtta cgggatcagc gttccttgtt
  61 gagtgggacc tgagttttga gagggtcttc tgctcctctt ggtctggtcc cttacttcca
 121 agagccccag agaggaaggc atgctgttgg ctctagctct gcttctagct ttcctgcctc
 181 ctgccagtca gaaatcttcc aacttggaag ggagaacaaa gtcagtcacc aggccaactg
 241 ggtcatcagc tgtaatcact tgtgatcttc ctgtagaaaa tgccgtctac acccactggt
 301 acctacacca ggaggggaag gccccacagc gtcttctgta ctatgactcc tacaactcca
 361 gggttgtgtt ggaatcagga atcagtcgag aaaagtatca tacttatgca agcacaggga
 421 agagccttaa atttatactg gaaaatctaa ttgaacgtga ctctggggtc tattactgtg
 481 ccacctggaa ggattattat aagaaactct ttggcagtgg aacaacactt gttgtcacag
 541 ataaacaact tgatgcagat gtttccccca agcccactat ttttcttcct tcgattgctg
 601 aaacaaaact ccagaaggct ggaacatatc tttgtcttct tgagaaattt ttcccagata
 661 ttattaagat acattggcaa gaaaagaaga gcaacacgat tctgggatcc caggagggga
 721 acaccatgaa gactaacgac acatacatga aatttagctg gttaacggtg ccagaagagt
 781 cactggacaa agaacacaga tgtatcgtca gacatgagaa taataaaaac ggaattgatc
 841 aagaaattat ctttcctcca ataaagacag atgtcaccac agtggatccc aaagacagtt
 901 attcaaaaga tgcaaatgat gtcaccacag tggatcccaa atacaattat tcaaaggatg
 961 caaatgatgt catcacaatg gatcccaaag acaattggtc aaaagatgca aatgatacac
1021 tactgctgca gctcacaaac acctctgcat attacatgta cctcctcctg ctcctcaaga
1081 gtgtggtcta ttttgccatc atcacctgct gtctgcttgg aagaacggct ttctgctgca
1141 atggagagaa atcataacag acggtggcac aaggaggcca tcttttcctc atcggttatt
1201 gtccctagaa gcgtcttctg aggatctagt tgggctttct ttctgggttt gggccatttc
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1261 agttctcatg tgtgtactat tctatcatta ttgtataatg gttttcaaac cagtgggcac

1321 acagagaacc tcagtctgta ataacaatga ggaatagcca tggcgatctc cagcaccaat

1381 ctctccatgt tttccacagc tcctccagcc aacccaaata gcgcctgcta tagtgtagac

1441 agcctgcggc ttctagcctt gtccctctct tagtgttctt taatcagata actgcctgga

1501 agcctttcat tttacacgcc ctgaagcagt cttctttgct agttgaatta tgtggtgtgt

1561 ttttccgtaa taagcaaaat aaattt
```

(see page 86, figure 3)

The alignment of SEQ ID NO: 3 and Littman is shown below:

```
Query Match            100.0%;  Score 20;  DB 5;  Length 1586;
  Best Local Similarity   100.0%;  Pred. No. 9.4;
  Matches   20;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps
0;

Qy          1 AGGGTTGTGTTGGAATCAGG 20
              ||||||||||||||||||||
Db        360 AGGGTTGTGTTGGAATCAGG 379
```

The alignment of the specific region of SEQ ID NO: 4 and Littman is shown below

```
Score = 46.8 bits (24),  Expect = 5e-04
 Identities = 24/24 (100%), Gaps = 0/24 (0%)
 Strand=Plus/Minus

Query  1    TGTTCCACTGCCAAAGAGTTTCTT  24
            ||||||||||||||||||||||||
Sbjct  524  TGTTCCACTGCCAAAGAGTTTCTT  501
```

As noted above, Tok teaches the use of a GC clamp with primers, such as SEQ ID NO: 4.

It would have been prima facie obvious to one of ordinary skill in the art at the

time the invention was made to use the TCR gamma sequence of Littman in the place of the sequence of Tok since both Tok and Littman teach analysis of TCR gene rearrangements (see page 454, column 2) and since Littman teaches that the sequence of figure 3 represents a known TCR gamma rearrangement (see page 87). An ordinary practitioner would have been motivated to amplify the sequence of Littman using primers such as those taught by Tok, with the GC clamp taught by Tok, from the published TCR gamma sequence of Littman in order to permit selection of primers with gene specificity and in order to perform the analytical methods of Tok.

In the court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

> "Normally, a *prima facie* case of obviousness is based upon structural similiarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties (see page 9, paragraph 4 of attached ref)."

Since the claimed PCR product simply represents a structural homolog, which are derived from sequences suggested by the prior art of Tok and Littman as useful for analysis of TCR gamma, and in particular for concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed PCR product, derived from the claimed primers of SEQ ID NO:s 3 and 4 are *prima facie* obvious over the cited references in the absence of secondary considerations.

Buck expressly provides evidence of the equivalence of primers. Specifically, Buck invited primer submissions from a number of labs (39) (page 532, column 3), with 69 different primers being submitted (see page 530, column 1). Buck also tested 95 primers spaced at 3 nucleotide intervals along the entire sequence at issue, thereby testing more than 1/3 of all possible 18 mer primers on the 300 base pair sequence (see page 530, column 1). When Buck tested each of the primers selected by the methods of the different labs, Buck found that EVERY SINGLE PRIMER worked (see page 533, column 1). Only one primer ever failed, No. 8, and that primer functioned when repeated. Further, EVERY SINGLE CONTROL PRIMER functioned as well (see page 533, column 1). Buck expressly states "The results of the empirical sequencing analysis were surprising in that nearly all of the primers yielded data of extremely high quality (page 535, column 2)." Therefore, Buck provides direct evidence that all primers would be expected to function, and in particular, all primers selected according to the ordinary criteria, however different, used by 39 different laboratories. It is particularly striking that all 95 control primers functioned, which represent 1/3 of all possible primers in the target region. This clearly shows that every primer would have a reasonable expectation of success.

Response to Arguments

8. Applicant's arguments filed January 16, 2007 have been fully considered but they are not persuasive.

Applicant argues that because Tok does not teach a "predetermined melting profile", Tok does not anticipate the claimed invention. The claimed invention is drawn

to a product. The Federal Circuit has repeatedly noted, most recently in Abbott Laboratories v. Baxter Pharmaceutical Products Inc., 80 USPQ2d 1860, 1863 (Fed. Cir. 2006) that "Our cases have consistently held that a reference may anticipate even when the relevant properties of the thing disclosed were not appreciated at the time." The Federal Circuit continues "The general principle that a newly-discovered property of the prior art cannot support a patent on that same art is not avoided if the patentee explicitly claims that property. "[A] prior art reference may anticipate without disclosing a feature of the claimed invention if that missing characteristic is necessarily present, or inherent, in the single anticipating reference." Id. at 1864. The composition of Tok inherently has a "melting profile". The attempt to import a purpose based distinction into a product claim will not render the product claim allowable. Therefore, Applicant's arguments with regard to the claims are not found persuasive.

Conclusion

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jeffrey Fredman
Primary Examiner
Art Unit 1637
2/6/07